REMARKS

Claims 1-11 and 14-23 are pending in the present application. Claims 15-17 were previously withdrawn from consideration by the Office. Claim 14 has been rejoined with the elected Group I for consideration. Claims 1-3, 5-8, 10, 11, and 18-22 have been amended herein to correct typographical errors. Upon entry of the present amendment, claims 1-11 and 14-23 will remain pending in this application.

Applicants note, with appreciation, that the Office did not repeat the rejection under 35 U.S.C. §112, second paragraph in the present Office Action. Accordingly, Applicants presume that this rejection has been withdrawn.

I. The Claimed Invention Is Not Obvious

Claims 1-10 and 14 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over PCT Publication No. WO98/28275 (hereinafter "Delorme") in view of Greene et. al., "Protective Groups in Organic Synthesis" (Third Edition, John Wiley & Sons, Inc., 1999) (hereinafter "Greene"). Applicants traverse the rejection and respectfully request reconsideration of the same.

Delorme does not teach or suggest the presently claimed invention. The Office points to the compound of Example 41 in Delorme that has an **unsubstituted** amino group on the phenyl ring (see, page 69 of Delorme), and alleges that it would be obvious to one skilled in the art to modify the unsubstituted amino group (see, Office Action at pages 6-7). The Office, however, does not explain why one skilled in the art would want to modify the unsubstituted amino group of the compound recited in Example 41 of Delorme.

One of ordinary skill in the art would not have been motivated to choose Applicants' particular substituted phenyl ring from the numerous variables reported for the A and B rings of Delorme, let alone been motivated to combine the substituted phenyl ring of the presently claimed invention with the R^1, R^2 and R^3 groups of the presently claimed invention. The Federal Circuit has made it clear that a claimed compound is not obvious over a prior art compound unless there is "a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound]…as a lead compound." *Takeda Chemical Industries, Ltd. v. Alphapharm*

Pty, Ltd., 492 F.3d 1350, 1357 (Fed. Cir. 2007) (finding a claimed compound non-obvious because one of ordinary skill in the art would not have selected the prior art compound as the lead compound out of the "hundreds of millions" of compounds disclosed by the prior art patent). The Office has not sufficiently identified a particular reason for selection of the compound of Example 41 of Delorme as a lead compound. Thus, claims 1-10 and 14 are not obvious over the Delorme reference. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. The Claimed Invention is Enabled

Claims 1-10, 14, and 18-23 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The Office alleges the specification:

> while being enabling for using the compounds of formula I with R1 equal to benzylaminocarbonyl, cyclopentyl, phenyl, cycloheptanyl, 2-chlorobenzoyl, 3-chlorobenzoyl, benzyl, 3-methylfuranyl, cyclohexyl, ethyl, 5-methylthien-2-yl)acetyl, 5-chlorothien-2-ylacetyl, 2-phenylpropanyl, 2-phenylbutanoyl, benzoyl, anilinocarbonyl, piperidinecarbonyl, piperidinylmethylsulfonyl, phenylethyl, cyclohexylethyl, dipropylcarbonyl, 1,2,3-benzotriazolecarbonyl; 1-methyl, 1,2,3-benzotriazolecarbonyl,3-pyridinecarbonyl, 2-methoxyphenylcarbonyl, 2-quinoxalinecarbonyl, 2,5-difluorophenylcarbonyl, 2-thiophenecarbonyl, methylphenylaminocarbonyl and wherein R1 and R2 come together to form a piperidine ring or pyrrolidine ring, R3 equal to hydrogen, and R2 equal to H, methyl, and ethyl, does not reasonably provide enablement for using the compounds of formula I where R1, R2, and R3 equal to any of the other moieties claimed.

(see, Office Action at pages 16-17). Applicants traverse the rejection and respectfully request reconsideration thereof because undue experimentation is not required to practice the claimed invention.

As will be recognized, the enablement requirement of §112 is satisfied as long as a disclosure contains a sufficient amount of information that persons of ordinary skill in the art having the disclosure before them are able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this

respect, the following statement from *In re Marzocchi*, is noteworthy:

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.
>
> … it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971).

The Office asserts that determining whether particular claimed compounds would be active "would require synthesis of the substrate and subjecting it to testing with Applicants' GTP binding assay" and "considering the large number of compounds to be made this is a large quantity of experimentation" (see, Office Action at page 18). Whether the amount of experimentation is large or small, however, is irrelevant to the determination of enablement. Moreover, even voluminous research is not undue so long as it is of a routine nature. *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Pat. Off. Bd. App. 1986). The Office has not alleged, let alone provided any support, that determining whether any particular claimed compound would be active by synthesizing the substrate and subjecting it to testing with Applicants' GTP binding assay amounts to undue experimentation.

In addition, Applicants have disclosed compounds and, in numerous cases, multiple compounds, with R moieties corresponding to those recited in the claims. Indeed, Applicants' specification does more than evidence an "intent" to make compounds; Applicants' specification discloses 12 synthesis schemes and 54 examples teaching how to make compounds in accordance with the claimed invention (see, pages 22-28 and 36-77 of the specification).

Accordingly, Applicants respectfully submit that the breath of the pending claims is reasonable.

The Office asserts "none of the working examples contains any radical R1-R3 equal to any of the moieties claimed other than the ones enabled above" (see, Office Action at page 18). Applicants remind the Office that a working example is not mandatory if none actually exists and the invention is otherwise disclosed so that one skilled in the art can practice it without undue experimentation. *In re Borkowski et al.*, 164 USPQ 642 (Fed. Cir. 1970); *In re Gay*, 135 U.S.P.Q. 311 (C.C.P.A. 1962); *In re Stephens*, 188 U.S.P.Q. 659 (C.C.P.A. 1976); and *Ex parte Krenzer*, 199 U.S.P.Q. 227 (Pat. Off. Bd. App. 1978). Moreover, Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art" for a generic claim to be fully enabled. See, *In re Angstadt*, 537 F.2d 498, 502 (C.C.P.A. 1976) (finding a generic claim enabled where the specification disclosed 40 examples).

The Office refers to PubMed Abstract 1281070 (hereinafter "the PubMed reference") and alleges that "[t]he state of the art is that the piperidinyl benzamide compound of cisapride has not been shown to have **sustained** positive effectiveness in the treatment of gastroparesis" (see, Office Action at page 18; emphasis added). Applicants respectfully point out that the enablement requirement does not require that all compounds have the same level of effectiveness. In this regard, the PubMed reference states that "[t]o some extent the therapeutic effectiveness of metoclopramide and cisapride has been established placebo-controlled trials" Further, the PubMed reference concludes that cisapride "be considered as a good alternative in cases where limited efficacy or side effect preclude the use of metoclopramide." Thus, Applicants respectfully submit that the PubMed reference actually supports the enablement of the present application because it confirms that cisapride is effective to at least some extent.

The Office states that the nature of the invention requires "an understanding of the receptor, the binding activity of small ligands to that receptor, and the ability of those compounds to module the delta opioid receptor" (see, Office Action at pages 18-19). No such "understanding" however, is required for enablement of the claimed invention. Indeed, one skilled in the art need not have any knowledge on how the claimed invention works. Rather, the enablement standard is whether undue experimentation is required to practice the claimed invention.

The Office asserts that there "is no reasonable basis for the assumption that the myriad of compounds embraced by the present formula (I) will share the same biological properties", and further asserts that there "is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity" (see, Office Action at page 19). Applicants respectfully disagree with such assertion especially in view of the teachings of the present application. Again, Applicants direct the Office to the Examples of compounds having one or more moieties for "R" groups recited in claim 1. Further, there is no requirement in the claims that the compounds "share the same biological properties."

In view of the foregoing, Applicants respectfully assert that the specification sufficiently enables one of skill in the art to use the claimed invention without undue experimentation. In light of the direction provided by 54 working examples in the specification, and disclosure of an example falling into many of the presently claimed R^1, R^2, and R^3 moieties, Applicants' respectfully assert that the presently claimed invention is enabled. Accordingly, Applicants respectfully request the rejection of claims 1-10, 14, and 18-23 under 35 U.S.C. §112, first paragraph, be withdrawn.

III. The Claimed Invention Is Clear And Definite

Claim 23 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office points to "Tf" in claim 23 (Applicants respectfully note that "-OTf" was correctly recited in claim 23 and in the specification, instead of "Tf" as alleged in the Office Action at page 22) and alleges its meaning is unclear and indefinite because there is no definition thereof provided in the claim. Applicants traverse the rejection and respectfully request reconsideration thereof.

As a preliminary matter, Applicants respectfully point out that the description of the invention is the role of the specification, not the claims. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081 (Fed. Cir. 1986). The proper inquiry, when determining whether a claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is a determination "whether those skilled in the art would understand what is claimed when the claim is read in

light of the specification." *Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986). To this end, one skilled in the art would understand that "-OTf" refers to trifluoromethanesulfonate (also known as triflate or [(trifluoromethyl)sulfonyl]oxy, the formula of which is CF_3SO_3-). The preparation of Intermediate 8 at page 65 and Scheme 12 at page 27 of the specification, for example, shows that "-OTf" means triflate (CF_3SO_3-). Thus, claim 23 is clear and definite. Accordingly, Applicants respectfully request the rejection of claim 23 under 35 U.S.C. §112, second paragraph, be withdrawn.

IV. Double Patenting Rejection

Claims 1, 5, 8, and 14 are provisionally rejected under 35 U.S.C. §101 over claim 23 of co-pending U.S. Patent Appl. No. 10/541,522 (hereinafter "the '522 application") as allegedly claiming the same invention. Applicants traverse the rejection and respectfully request reconsideration thereof.

Claims 1, 5, 8, and 14 of the present application are not directed to the "same invention" as that of claim 23 of the '522 application. "Same invention" means identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1984); *In re Ockert*, 114 U.S.P.Q. 330 (C.C.P.A. 1957); and *In re Vogel*, 164 U.S.P.Q. 619 (C.C.P.A. 1970). As stated in §804 of the M.P.E.P., if there is an embodiment of the invention that falls within the scope of one claim but not the other, then "identical subject matter **is not** defined by both claims and statutory double patenting would not exist" (emphasis added). Since the scope of the rejected claims in the present application and the '522 application differ, statutory double patenting is precluded. Accordingly, Applicants respectfully request the rejection of claims 1, 5, 8, and 14 under 35 U.S.C. §101 over claim 23 of the '522 application be withdrawn.

Claims 1, 5, 8, and 14 are provisionally rejected under 35 U.S.C. §101 over claim 22 of co-pending U.S. Patent Appl. No. 10/541,656 (hereinafter "the '656 application") as allegedly claiming the same invention. Applicants traverse the rejection and respectfully request reconsideration thereof.

Claims 1, 5, 8, and 14 of the present application are not directed to the "same invention" as that of claim 22 of the '656 application. As stated above, "Same invention" means identical

subject matter. *Id.* Since the scope of the rejected claims in the present application and the '656 application differ, statutory double patenting is precluded. Accordingly, Applicants respectfully request the rejection of claims 1, 5, 8, and 14 under 35 U.S.C. §101 over claim 22 of the '656 application be withdrawn.

V. Nonstatutory Obviousness-Type Double Patenting Rejections

Claims 1, 2, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4 and 8 of co-pending U.S. Patent Publ. No. 2007/0099957 (hereinafter "the '957 publication"), and claims 11 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claim 5 of the '957 publication. Claims 1, 2, 11, and 14 are also rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-5 and 8 of U.S. Patent Appl. No. 10/555,980 (published as U.S. Patent Publ. No. 2007/0099957, for clarity purpose, hereinafter also referred as "the '957 publication").

Applicants respectfully submit that the present application is a §371 application of PCT Appl. No. PCT/SE2003/001705 filed November 5, 2003, whereas the '957 publication is a §371 application of PCT Appl. No. PCT/GB2004/002074 filed May 13, 2004. As such, the present application is the earlier filed of the applications. Although Applicants disagree with the reasoning set forth by the Office, Applicants respectfully assert that when a "provisional" nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of two pending applications, the Office should withdraw the obviousness-type double patenting rejection in the earlier filed case and permit it to issue without requiring a terminal disclaimer.

Claims 1, 6, 7, 8, 10, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 4, 8, 15, 16, and 18 of co-pending U.S. Patent Appl. No. 10/596,850 (hereinafter "the '850 application") in view of the Greene reference.

Applicants respectfully submit that the present application is a §371 application of PCT Appl. No. PCT/SE2003/001705 filed November 5, 2003, whereas the '850 application is a §371 application of PCT Appl. No. PCT/SE2005/000012 filed January 15, 2005. As such, the present

application is the earlier filed of the applications. Although Applicants disagree with the reasoning set forth by the Office, Applicants respectfully assert that when a "provisional" nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of two pending applications, the Office should withdraw the obviousness-type double patenting rejection in the earlier filed case and permit it to issue without requiring a terminal disclaimer.

Claims 1, 5, 8, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4, 8, 13, and 19-22 of the '522 application in view of the Greene reference. Claims 1, 5, 8, and 14 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claim 13 of the '522 application.

Applicants respectfully submit that the present application is a §371 application of PCT Appl. No. PCT/SE2003/001705 filed November 5, 2003, whereas the '850 application is a §371 application of PCT Appl. No. PCT/GB2004/000099 filed January 13, 2004. As such, the present application is the earlier filed of the applications. Although Applicants disagree with the reasoning set forth by the Office, Applicants respectfully assert that when a "provisional" nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of two pending applications, the Office should withdraw the obviousness-type double patenting rejection in the earlier filed case and permit it to issue without requiring a terminal disclaimer.

Claims 1, 5, 8, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-5, 8, and 19-21 of the '656 application in view of the Greene reference. Claims 1, 5, 8, and 14 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claim 12 of the '656 application.

Applicants respectfully submit that the present application is a §371 application of PCT Appl. No. PCT/SE2003/001705 filed November 5, 2003, whereas the '850 application is a §371 application of PCT Appl. No. PCT/GB2004/000116 filed January 13, 2004. As such, the present application is the earlier filed of the applications. Although Applicants disagree with the reasoning set forth by the Office, Applicants respectfully assert that when a "provisional" nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the

earlier filed of two pending applications, the Office should withdraw the obviousness-type double patenting rejection in the earlier filed case and permit it to issue without requiring a terminal disclaimer.

VI. Conclusion

Applicants respectfully submit the claims are in condition for allowance. An early notice of same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at 610.640.7859 if there are any questions regarding the captioned application.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

/Paul K. Legaard, Reg.# 38534/
Paul K. Legaard, Ph.D.

Date: **7 November 2008**

Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

Telephone: 610.640.7859
Facsimile: 267.430.7647